Pharmacology Biochemistry & Behavior, Vol. 34, pp. 811–816. © Pergamon Press plc, 1989. Printed in the U.S.A. 0091-3057/89 $3.00 + .00

Inhibitory Action of Various 5-HT_{1B} Receptor Agonists on Rat Masculine Sexual Behaviour

A. FERNÁNDEZ-GUASTI,*[1] A. ESCALANTE* AND A. ÅGMO†

**Sección de Terapéutica Experimental, Departamento de Farmacología y Toxicología CINVESTAV and División de Investigaciones en Neurociencias, Instituto Mexicano de Psiquiatría and †Escuela de Psicología, Universidad Anahuac, México D.F., México*

Received 28 November 1988

FERNÁNDEZ-GUASTI, A., A. ESCALANTE AND A. ÅGMO. *Inhibitory action of various 5-HT_{1B} receptor agonists on rat masculine sexual behaviour.* PHARMACOL BIOCHEM BEHAV **34**(4) 811–816, 1989.—The systemic administration of the 5-HT_{1B} receptor agonists, RU 24969 (0.25 and 0.5 mg/kg), TFMPP (0.25 and 0.5 mg/kg) and mCPP (0.75 and 1.0 mg/kg) resulted in an inhibition of rat masculine sexual behaviour reflected as a reduction in the proportion of copulating animals. Additionally, the analysis of the sexual behaviour of the animals obtaining ejaculation revealed that RU 24969 and TFMPP administration resulted in an increase in the number of mounts and in a prolongation of the intromission and ejaculation latencies and of the postejaculatory interval. Administration of mCPP increased the number of mounts preceding ejaculation. None of these changes could be attributed to a motor coordination impairment since none of these drugs, at the doses tested, produced changes in a treadmill test. The administration of the 5-HT_{1A} agonist, ipsapirone (2.5, 5 and 10 mg/kg) resulted in a facilitation of the sexual behaviour expressed as a reduction in the number of intromissions preceding ejaculation accompanied by a shortening of the ejaculation latency. Present data show a differential action of 5-HT_{1A} and 5-HT_{1B} receptor subtypes in the control of rat masculine sexual behaviour. The hypothesis that the endogenous serotonin inhibitory action on copulation is mediated via the 5-HT_{1B} receptor subtype is proposed.

Rat masculine sexual behaviour RU 24969 TFMPP mCPP Ipsapirone 5-HT_{1A} and 5-HT_{1B} receptor subtypes

IT has been demonstrated that the administration of the serotonin (5-HT) precursor, 5-hydroxytryptophan (5-HTP), and of the 5-HT reuptake inhibitor, chlorimipramine, results in an inhibition of masculine sexual behaviour (3, 4, 23). Opposite effects have been described after electrolytic or neurotoxic lesions of the raphé nucleus (22,24) or after administration of the 5-HT synthesis inhibitor, p-chlorophenylalanine (pCPA) (2,33). These data led to the conclusion that the serotonergic system plays an inhibitory role in the neural control of rat male sexual behaviour.

On the basis of the affinity of various agonists and antagonists, several 5-HT binding sites have been established [cf. (29)]. Thus, in the rat central nervous system, the 5-HT_{1A}, 5-HT_{1B} and 5-HT_2 binding sites have been recognized (20, 21, 30). It has been demonstrated that administration of 5-HT_{1A} agonists results in a facilitation of male sexual behaviour reflected as a reduction in the number of intromissions preceding ejaculation accompanied by a decrease in the ejaculation latency (5–8, 15, 17, 19). Additionally, the administration of 5-HT_2 antagonists causes an inhibition of copulation (26). These data have led to the suggestion that both 5-HT_{1A} and 5-HT_2 receptor types mediate a facilitatory action on copulatory behaviour.

In view that 5-HT may also bind to the 5-HT_{1B} sites, it is hypothesized that this receptor subtype mediates the inhibitory action of endogenous 5-HT. A first attempt to demonstrate this hypothesis consisted in the analysis of the sexual behaviour after the administration of various 5-HT_{1B} agonists and to compare their action with that induced by the 5-HT_{1A} agonist, ipsapirone. In order to exclude the possibility that a nonspecific motor impairment mediates the effects of these drugs, the motor coordination was evaluated in a rotarod (treadmill) test.

METHOD

Animals

Sexually experienced adult male Wistar rats (250–350 g body weight) were used. Animals were housed six per cage in a room with controlled light:dark cycle (12-hr light:12 hr dark, lights on at 2200 hr). All animals had free access to water and Purina rat chow over all the experiments.

Animals were castrated under methoexital (40 mg/kg) anesthesia and subcutaneously implanted with a Silastic capsule (20 mm

[1]Requests for reprints should be addressed to Dr. Alonso Fernández-Guasti, Sección de Terapéutica Experimental, Departamento de Farmacología y Toxicología, Ap. Postal 22026, México 14000 D.F., México.

long, 0.062 in. internal diameter and 0.125 in. external diameter, Dow Corning) filled with testosterone (Sigma Chemicals, St. Louis, MO) as previously described (1). Three days after castration the animals were retested for sexual behaviour and only those animals ejaculating within a 30-min period were included for further experimentation.

Drugs

The following drugs were used in this study: RU 24969 [5-methoxy-3-(1,2,3,6-tetrahydro-4-pyridinyl) indole], TFMPP [1-(m-trifluoromethylphenyl)piperazine], mCPP [1-(m-chlorophenyl) piperazine], and ipsapirone. TFMPP and mCPP were purchased from Research Biochemicals Inc., RU 24969 and ipsapirone were kindly donated by Roussell Uclaf and Tropon Chemistry Department, respectively. All drugs were dissolved in physiological saline and IP injected in a volume of 2.0 ml/kg.

Sexual Behaviour Observations

Sexual behaviour observations were begun two hours after the onset of darkness. The males were presented with a female brought into sexual receptivity by the sequential administration of oestrogen followed 48 hr later by progesterone, that was administered 6 hr before testing. During the test the following parameters were recorded: intromission latency, number of mounts and intromissions preceding ejaculation, ejaculation latency and postejaculatory interval [for definition of each behavioural item see Larsson and Ahlenius (23)]. Mount, intromission and ejaculation were recognized because of their particular behavioural characteristics. Tests were concluded at the end of the postejaculatory interval or 30 min after the introduction of the female if no ejaculation occurred.

Procedure

RU 24969 (0, 0.125, 0.25 and 0.5 mg/kg), TFMPP (0, 0.125, 0.25 and 0.5 mg/kg), mCPP (0, 0.5, 0.75 and 1.0 mg/kg) and ipsapirone (0, 2.5, 5.0 and 10.0 mg/kg) were administered according to a balanced latin square design in such a way that each animal received all treatments.

Motor Coordination Test (Treadmill Test)

After sexual behaviour observations all animals were tested for motor coordination in a treadmill apparatus (rotarod). The procedure followed was the same as previously described by Ågmo *et al.* in 1987 (1). Briefly, this test consisted of placing trained animals upon a cylinder (diameter 7 cm) rotating at a speed of 11 rpm. After saline or different doses of the 5-HT_{1A} or 5-HT_{1B} agonists used, the number of falls during a 5-min period was counted. After a fall the animal was immediately replaced upon the cylinder.

Statistical Analysis

The proportion of animals showing mounts, intromissions or ejaculation was evaluated using the Cochran's Q-test followed by the binomial test (34). The specific sexual behaviour parameters were analyzed using the Friedman's two-way analysis of variance followed by the Wilcoxon matched-pairs signed-ranks test (34). The treadmill test data were statistically analyzed using the Wilcoxon matched-pairs signed-ranks test (34).

RESULTS

The results obtained after the administration of the 5-HT_{1A} receptor agonists used in this study, ipsapirone, are shown in Table 1. All animals treated with ipsapirone displayed copulatory behaviour. As expected, a clear dose-dependent reduction in the number of intromissions preceding ejaculation accompanied by a reduction in the ejaculation latency was found.

TABLE 1

EFFECT OF IPSAPIRONE ON RAT MASCULINE SEXUAL BEHAVIOUR

Treatment (mg/kg)	IL	NM	NI	EL	PEI
Saline	0.4	7	12	9.6	6.5
Ipsapirone (2.5)	0.6	6	6*	4.0*	6.2
Ipsapirone (5.0)	0.2	4	6*	3.6†	5.6
Ipsapirone (10.0)	1.3	6	5†	2.2†	6.9
χ^{2a}	1.05	1.76	12.60	9.15	5.25
$p<$	n.s.	n.s.	0.006	0.027	n.s.

Table shows median values. The analysis was made on the basis of the performance of eight animals. IL, intromission latency; NM, number of mounts; NI, number of intromissions; EL, ejaculation latency, and PEI, postejaculatory interval. The statistical analysis was made between the control (saline)- and the experimental (ipsapirone)-treated groups. [a]Friedman two-way analysis of variance; Wilcoxon matched-pairs signed ranks test, *$p<0.05$; †$p<0.02$.

The results showing the effect on the copulatory behaviour of the various 5-HT_{1B} receptor agonists are shown in Tables 2–4 and Fig. 1. In all experiments the saline-treated animals showed the complete behavioural repertoire of copulation. Treatment with the low dose of RU 24969 (0.125 mg/kg) induced a slight nonstatistically significant decrease in the proportion of animals displaying

TABLE 2

EFFECT OF RU 24969 ON RAT MASCULINE SEXUAL BEHAVIOUR

Treatment (mg/kg)	N	IL	NM	NI	EL	PEI
Control	9	0.3	3	9	6.3	7.0
RU 24969 (0.125)	9	0.4	10	10	9.4	7.1
Control	6	0.1	3	10	6.3	5.8
RU 24969 (0.25)	6	1.2*	24*	13	12.4	7.5*
Control	4	0.1	3	8	2.5	5.4
RU 24969 (0.5)	4	1.0	15	9	12.3	7.7

Table shows median values. The analysis is based only in those animals that obtained ejaculation after the treatment. Abbreviations as in Table 1. The statistical comparisons were made between the animals that ejaculated and their respective saline-treated values. At the highest dose no statistical analysis was performed due to the fact that only 4 animals ejaculated after this dose. Wilcoxon matched-pairs signed-ranks test, *$p<0.05$.

TABLE 3

EFFECT OF TFMPP ON RAT MASCULINE SEXUAL BEHAVIOUR

Treatment (mg/kg)	N	IL	NM	NI	EL	PEI
Control	8	0.4	5	7	5.0	5.9
TFMPP (0.125)	8	0.2	2	7	4.5	5.5
Control	8	0.6	5	7	5.0	5.9
TFMPP (0.25)	8	0.8	12*	7	7.7	6.0
Control	3	0.6	6	8	6.6	5.9
TFMPP (0.5)	3	4.3	17	7	17.4	6.1

Table shows median values. The analysis is based only in those animals that obtained ejaculation after the treatment. Abbreviations as in Table 1. The statistical analysis was made between the animals that ejaculated and their respective saline-treated values. After the highest dose no statistical analysis was made since only 3 animals ejaculated. Wilcoxon matched-pairs signed-ranks test, *$p<0.02$.

TABLE 4

EFFECT OF mCPP ON RAT MASCULINE SEXUAL BEHAVIOUR

Treatment (mg/kg)	N	IL	NM	NI	EL	PEI
Control	8	0.2	4	10	4.1	4.7
mCPP (0.5)	8	0.4	2	8	5.4	5.3
Control	6	0.2	4	10	4.4	4.7
mCPP (0.75)	6	0.5	4	9	7.7	6.0
Control	3	0.2	4	12	4.8	4.3
mCPP (1.0)	3	0.3	7	11	9.4	5.6

Table shows median values. The analysis is based only in those animals that obtained ejaculation after the treatment. Abbreviations as in Table 1. The statistical analysis was made between the animals that ejaculated and their respective saline-treated values. No statistical analysis was performed after the highest dose since only 3 animals ejaculated. Wilcoxon matched-pairs signed-ranks test, nonsignificant.

ejaculation. Higher doses of RU 24969 resulted in a dose-dependent inhibition of sexual behaviour. Thus, after administration of 0.25 mg/kg or 0.5 mg/kg only 42% or 33%, respectively, of the animals ejaculated (Fig. 1). Table 2 compares the various sexual behaviour parameters after the administration of the different doses of RU 24969. The analysis is based only on the performance of those animals that obtained ejaculation. A tendency for an increase in the number of mounts and ejaculation latency was found after the administration of 0.125 mg/kg. The injection of 0.25 mg/kg produced a statistically significant increase in the following parameters: number of mounts, number of intromissions, ejaculation latency and postejaculatory interval. After the highest dose (0.5 mg/kg) a drastic inhibition of copulation was found (i.e., only 4 animals ejaculated). Thus, the Wilcoxon *t*-test could not be applied for analyzing the data. It is worth noting, however, that this dose produced similar changes to those observed after 0.25 mg/kg.

Figure 1 also shows the proportion of copulating animals after the administration of TFMPP. Clearly, a dose-dependent inhibition of the sexual behaviour was found. Thus, after the administration of 0.125 or 0.25 mg/kg almost all animals copulated, while a higher dose, 0.5 mg/kg, resulted in a decrease of copulating animals (only 38% of the animals ejaculated). Table 3 shows the analysis of the various sexual behaviour parameters. The injection of 0.125 mg/kg did not modify any parameter. However, 0.25 mg/kg TFMPP produced an increase in the number of mounts

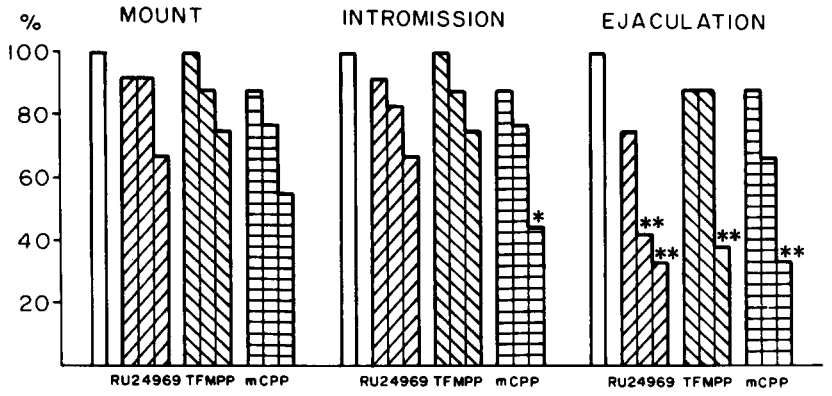

FIG. 1. Percentage of animals showing mounts, intromissions or ejaculation during a 30-min copulating test, after the administration of various doses of the 5-HT$_{1B}$ agonists, RU 24969 (0.125, 0.25 and 0.5 mg/kg), TFMPP (0.125, 0.25 and 0.5 mg/kg) and mCPP (0.5, 0.75 and 1.0 mg/kg). Open bars represent respective control values, dashed bars represent ascendent dosages of the compounds showed in figure. Cochran Q values: RU 24969 (N = 12): mounts, 7.0, n.s., intromissions, 8.0, $p<0.05$, ejaculation, 14.4, $p<0.01$; TFMPP (n = 8): mounts, 2.0 n.s., intromissions, 2.0, n.s., ejaculation, 9.32, $p<0.05$; mCPP (n = 9): mounts, 8.07, $p<0.05$, intromissions, 10.5, $p<0.02$, ejaculation, 12.75, $p<0.01$. Binomial test, *$p<0.05$; **$p<0.02$.

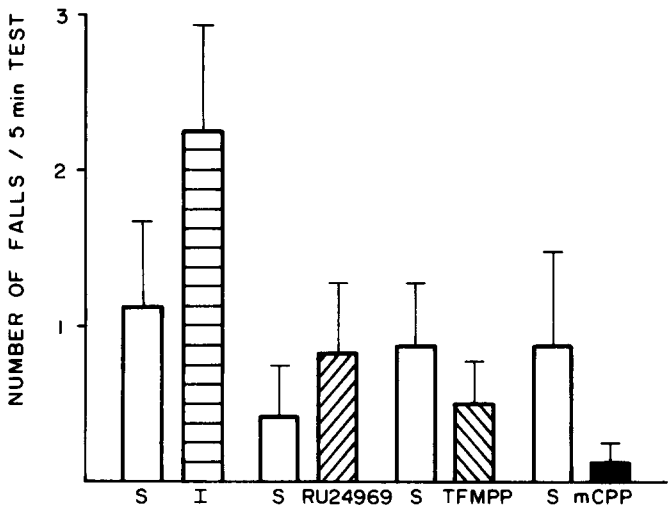

FIG. 2. Motor coordination test after administration of ipsapirone (10 mg/kg), RU 24969 (0.5 mg/kg), TFMPP (0.5 mg/kg) or mCPP (1.0 mg/kg). Figure shows means ± S.E. number of falls during a 5-min treadmill test. Wilcoxon matched pairs signed-ranks test, $p>0.05$, non-significant.

preceding ejaculation. No other parameter was altered after this dose. After the highest dose used (0.5 mg/kg) an increase in the number of mounts accompanied by a prolongation in the intromission and ejaculation latencies was found. This analysis, however, is based only on the performance of three animals.

Table 4 and Fig. 1 show the effect of mCPP on sexual behaviour. After the administration of low doses (0.5 and 0.75 mg/kg) the proportion of copulating animals was slightly altered. However, the injection of 1.0 mg/kg resulted in a decrease in the proportion of animals showing sexual behaviour (44 and 33% of the animals treated with this dose intromitted and ejaculated, Fig. 1). As to the analysis of the various parameters, 0.5 mg/kg of mCPP did not produce any effect, while 0.75 mg/kg slightly prolonged the ejaculation latency. After the administration of the highest dose (1.0 mg/kg) an increase in the number of mounts and in the ejaculation latency was found (Table 3). No statistical analysis could be performed since only 3 out of 9 animals ejaculated.

The results of the motor coordination test are shown in Fig. 2. This figure shows the data after administering the highest doses used for each compound. None of the compounds, at the doses tested, resulted in a motor coordination impairment.

DISCUSSION

Present data show that, as previously reported (19), the administration of the new 5-HT_{1A} receptor agonist, ipsapirone, induced a reduction in the number of intromissions preceding ejaculation accompanied by a shortening of the ejaculation latency. Present results also show that all the 5-HT_{1B} receptor agonists used (RU 24969, TFMPP and mCPP) dose-dependently inhibited the copulatory behaviour without interfering with the motor coordination.

It is well established that the administration of 5-HT_{1A} agonists 8-OH-DPAT (6, 8, 23), 5 Me-ODMT (15), lisuride (5, 7, 15) and indorenate (17) produces a reduction in the number of intromissions preceding ejaculation accompanied by a reduction in the ejaculation latency. Present data showing that ipsapirone, a well characterized 5-HT_{1A} receptor agonist (12, 19, 36), produces the same effects as the other 5-HT_{1A} receptor agonists, support the idea that this receptor subtype serves a facilitatory role in the copulatory behaviour, mainly by regulating the number of intromissions preceding ejaculation and thereby the ejaculation latency.

In the analysis of the role of 5-HT on female sexual behaviour it has been proposed that the 5-HT_{1A} receptor subtype mediates an inhibitory action, while the 5-HT_{1B} could be involved in a presynaptic facilitatory mediation (16,27). Additionally, Mendelson and Gorzalka (26,28) have established that the 5-HT_{1A} receptor subtype possesses a differential function on male and female sexual behaviour and suggested that in the former the 5-HT_{1B} receptor subtype could mediate an inhibitory action. Present results give experimental support to this proposition and indicate that these receptor subtypes play opposite roles in the control of rat masculine sexual behaviour.

Interestingly, it has been reported that the 5-HT_{1A} agonists inhibit seminal emission and ejaculation ex copula (9,31), while the 5-HT_{1B} agonists stimulate these responses (9,32). These data indicate that the different 5-HT_1 receptor subtypes serve opposite roles in the control of spontaneous seminal emission. Additionally, it has been suggested (11) that drugs that inhibit the ex copula reflexes facilitate the sexual behaviour by reducing the ejaculation threshold; by contrast, drugs that facilitate the ex copula reflexes may inhibit the sexual behaviour. Present data, together with previous results (9,32) showing that the 5-HT_{1B} agonists facilitate the spontaneous seminal emission and inhibit copulation, while 5-HT_{1A} agonists inhibit the penile reflexes and the spontaneous seminal emission, and facilitate sexual behaviour, are in line with the above proposed hypothesis. Additionally, these data support the notion of a differential role of these receptor subtypes in the mediation of sexual reflexes, spontaneous seminal emission and copulatory behaviour.

Although RU 24969 has been proposed as a selective 5-HT_{1B} receptor agonist (21,37), it has recently been reported that RU 24969 may induce several behavioural characteristics associated with the stimulation of the 5-HT_{1A} receptor subtype (18,37). Masculine sexual behaviour, due to its complexity, has to be cautiously considered as a paradigm to establish behavioural drug characteristics. However, present results showing a clear differential effect of 5-HT_{1A} and $_B$ receptor agonists on copulation, make it possible to propose this behaviour as a useful tool to differentiate between both agonists classes. Needless to mention, besides copulation, other behavioural parameters must be considered before proposing a drug as a 5-HT_{1A} or $_B$ agonist.

The 5-HT_{1B} receptor subtype has low affinity for spiperone and can be selectively labelled with (−) (^{125}I) iodocyanopindolol (20, 21, 30). Binding studies have reported that the most potent agonists for the 5-HT_{1B} receptor are RU 24969 and TFMPP followed by mCPP and quipazine (35). Interestingly, we have observed that RU 24969 and TFMPP were the most potent drugs to inhibit the masculine sexual behaviour followed by mCPP and quipazine (26). These data suggest that the inhibition of this behaviour is mediated through the action of these drugs at the 5-HT_{1B} receptor subtype. The 5-HT_1 blocking agents are nonselective, not only within the different classes of this binding site, but also antagonize the beta adrenergic [(−) pindolol, (−) alprenolol] or the 5-HT_2 receptor (metiotepine, metergoline). In relation with the later group of drugs, it has to be considered that after blocking the 5-HT_2 site, an inhibition of the sexual behaviour occurs (26). In spite of these disadvantages, further experiments using these antagonists should be made.

Recently, it has been shown that 5-HT_{1A} and $_{1B}$ receptors have different brain localization. While the 5-HT_{1A} receptor subtype is mainly located in the hippocampal formation, cerebral cortex and nucleus raphé dorsalis, the 5-HT_{1B} receptor is primarily concentrated in the globus pallidus, dorsal subiculum and substantia nigra

(10, 20, 29). These localization differences could at least partly explain the different role that the receptor subtypes play in the control of masculine sexual behaviour. Further experiments, using local brain injection of these agonists, should be made in order to further explore this possibility.

It has been proposed that the 5-HT$_{1B}$ binding site could mediate presynaptic actions of 5-HT (13, 14, 25). However, the presence of these binding sites in the postsynaptic fraction has also been demonstrated (20,21). From present data it could not be assumed whether these drugs stimulate pre- or postsynaptic receptors; however, most likely the effect of these drugs on masculine sexual behaviour seem to be mediated via a postsynaptic action. Furthermore, from present results it could be proposed that endogenous 5-HT act at the same receptor subtype, as the drugs used in this study, to inhibit rat masculine sexual behaviour. Further experimentation to confirm this idea should be undertaken.

ACKNOWLEDGEMENTS

The authors wish to thank the pharmaceutical companies Rousell Uclaf and Troponwerke for the kind donation of RU 24969 and ipsapirone respectively. The authors also are thankful to Dr. Julian Davidson for valuable comments to the manuscript.

REFERENCES

1. Ågmo, A.; Paredes, R.; Fernández, H. Differential effects of GABA transaminase inhibitors on sexual behaviour, locomotor activity and motor execution in the male rat. Pharmacol. Biochem. Behav. 28:47–52; 1987.
2. Ahlenius, S.; Eriksson, H.; Larsson, K.; Modigh, K.; Södersten, P. Mating behaviour in the male rat treated with p-chlorophenylalanine methyl esther alone and in combination with pargyline. Psychopharmacologia 20:383–388; 1971.
3. Ahlenius, S.; Heiman, M.; Larsson, K. Prolongation of the ejaculation latency in the male rat by thioridazine and chlorimipramine. Psychopharmacology (Berlin) 65:137–140; 1979.
4. Ahlenius, S.; Larsson, K.; Svensson, L. Further evidence for an inhibitory role of central 5-HT in male rat sexual behaviour. Psychopharmacology (Berlin) 68:217–220; 1980.
5. Ahlenius, S.; Larsson, K.; Svensson, L. Stimulating effects of lisuride on masculine sexual behaviour of rats. Eur. J. Pharmacol. 64:47–51; 1980.
6. Ahlenius, S.; Larsson, K.; Svensson, L.; Hjorth, S.; Carlsson, A.; Lindberg, P.; Wikström, H.; Sánchez, D.; Arvidsson, L.-E.; Hacksell, U.; Nilsson, J. L. G. Effects of a new type of 5-HT receptor agonist on male rat sexual behaviour. Pharmacol. Biochem. Behav. 15:785–792; 1981.
7. Ahlenius, S.; Larsson, K. Lisuride, LY-141865 and 8-OH-DPAT facilitate male rat sexual behaviour via a non-dopaminergic mechanism. Psychopharmacology (Berlin) 83:330–334; 1984.
8. Ahlenius, S.; Larsson, K. Evidence for a unique pharmacological profile of 8-OH-DPAT by evaluation of its effects on male rat sexual behaviour. In: Dourish, C. T.; Ahlenius, S.; Hutson, P., eds. Brain 5-HT1A receptors: Behavioural and neurochemical pharmacology. Chichester: Ellis Horwood Ltd.; 1987:186–198.
9. Berendsen, H. H. G.; Broekkamp, C. L. E. Drug-induced penile erection in rats: indications of serotonin 1B receptor mediation. Eur. J. Pharmacol. 135:279–287; 1987.
10. Cortés, R.; Palacios, J. M.; Pazos, A. Visualization of multiple serotonin receptors in the rat brain by autoradiography. Br. J. Pharmacol. 81:202P; 1984.
11. Davidson, J. M.; Smith, E. R.; Lee, R. L.; Schnur, S. L. Sexual dissonance: drugs stimulate sexual arousal and/or lower ejaculatory threshold, while suppressing erectile and ejaculatory responses ex copula. XIX Conference on Reproductive Behaviour, México; 1987: 15.
12. Dompert, W. U.; Glaser, T.; Traber, J. ^{3}H-TVX Q 7821: Identification of 5-HT1 binding sites as a target for a novel putative anxiolytic. Naunyn Schmiedebergs Arch. Pharmacol. 328:467–470; 1985.
13. Engel, G.; Göthert, M.; Müller-Schweinitzer, E.; Schlicker, E.; Sistonen, L.; Stadler, P. A. Evidence for common pharmacological properties of (3H) 5-hydroxytryptamine binding sites, presynaptic 5-hydroxytryptamine autoreceptors in CNS and inhibitory presynaptic 5-hydroxytryptamine receptors in sympathetic nerves. Naunyn Schmiedebergs Arch. Pharmacol. 324:116–124; 1983.
14. Engel, G.; Göthert, M.; Hoyer, D.; Schlicker, E.; Hillenbrand, K. Identity of inhibitory presynaptic 5-hydroxytryptamine (5-HT) autoreceptors in the rat brain cortex with 5-HT1B binding sites. Naunyn Schmiedebergs Arch. Pharmacol. 332:1–7; 1986.
15. Fernández-Guasti, A.; Hansen, S.; Archer, T.; Jonsson, G. Noradrenaline-serotonin interactions in the control of sexual behaviour in the male rat: DSP4-induced noradrenaline depletion antagonizes the facilitatory effect of the serotonin receptor agonist 5MeODMT and lisuride. Brain Res. 377:112–118; 1986.
16. Fernández-Guasti, A.; Ahlenius, S.; Hjorth, S.; Larsson, K. Separation of dopaminergic and serotonergic inhibitory mechanisms in the mediation of estrogen-induced lordosis behaviour in the rat. Pharmacol. Biochem. Behav. 27:93–98; 1987.
17. Fernández-Guasti, A.; Escalante, A.; Ågmo, A.; Hong, E. Behavioural actions of indorenate, a new putative 5-HT receptor agonist. Submitted.
18. Gardner, C. R.; Guy, A. P. Behavioural effects of RU 24969, a new putative 5-HT1 agonist in the mouse. Br. J. Pharmacol. 78:96P; 1983.
19. Glaser, T.; Dompert, W. U.; Schuurman, T.; Spencer, D. G., Jr.; Traber, J. Differential pharmacology of the novel 5-HT1A receptor ligands 8-OH-DPAT, BAY R 1531 and ipsapirone. In: Dourish, C. T.; Ahlenius, S.; Hutson, P., eds. Brain 5-HT1A receptors: Behavioural and neurochemical pharmacology. Chichester: Ellis-Horwood Ltd.; 1987:106–119.
20. Hoyer, D.; Engel, G.; Kalman, H. Characterization of the 5-HT1B recognition site in the rat brain: binding studies with (−) (125I) iodocyanopindolol. Eur. J. Pharmacol. 118:1–12; 1985.
21. Hoyer, D.; Engel, G.; Kalman, H. Molecular pharmacology of 5-HT1 and 5-HT2 recognition sites in rat and pig brain membranes: radioligand binding studies with (3H) 5-HT, (3H) 8-OH-DPAT, (−) (125I) iodocyanopindolol, (3H) mesulergine and (3H) ketanserin. Eur. J. Pharmacol. 118:13–23; 1985.
22. Larsson, K.; Fuxe, K.; Everitt, B. J.; Holmgren, M.; Södersten, P. Sexual behaviour in male rats after intracerebral injection of 5,7 dihydroxytryptamine. Brain Res. 141:293–303; 1978.
23. Larsson, K.; Ahlenius, S. Masculine sexual behaviour and brain monoamines. In: Segal, M., ed. Psychopharmacology of sexual disorders. London: John Libbey; 1986.
24. McIntosh, T. K.; Barfield, R. J. Brain monoaminergic control of male reproductive behaviour. I. Serotonin and the postejaculatory refractory period. Behav. Brain Res. 12:255–265; 1984.
25. Martin, L. L.; Sanders-Bush, E. Comparison of the pharmacological characteristics of 5-HT1 and 5-HT2 binding sites with those of serotonin autoreceptors which modulate serotonin release. Naunyn Schmiedebergs Arch. Pharmacol. 321:165–170; 1982.
26. Mendelson, S. D.; Gorzalka, B. B. Serotonin antagonist pirenperone inhibits sexual behaviour in the male rat: Attenuation by quipazine. Pharmacol. Biochem. Behav. 22:565–571; 1985.
27. Mendelson, S. D.; Gorzalka, B. B. 5-HT1A receptors: Differential involvement in female and male sexual behaviour in the rat. Physiol. Behav. 37:345–351; 1986.
28. Mendelson, S. D.; Gorzalka, B. B. Differential roles of 5-HT receptor subtypes in female sexual behaviour. In: Archer, T.; Bevan, P.; Cools, L. L., eds. Behavioural pharmacology of serotonin. New York: Lawrence Erlbaum; 1987.
29. Pazos, A.; Palacios, J. M. Quantitative autoradiographic mapping of serotonin receptors in the rat brain. I: Serotonin 1 receptors. Brain Res. 346:205–230; 1985.
30. Peroutka, S. J. 5-HT1 receptor sites and functional correlates. Neuropharmacology 23:1487–1492; 1984.
31. Rény, L., Ejaculations induced by p-chloroamphetamine in the rat. Neuropharmacology 24:697–704; 1985.
32. Rény, L.; Lewander, T. 5-HT1A and 5-HT1B agonists produce opposite effect on the ejaculatory response induced by amphetamine in

rats. Behavioural Pharmacology of 5-HT. International Congress, Amsterdam; 1987:34.
33. Salis, P. J.; Dewsbury, D. A. p-Chlorophenylalanine facilitates copulatory behaviour in male rats. Nature 232:400–401; 1979.
34. Siegel, S. Non-parametric statistics for the behavioural sciences. New York: McGraw Hill; 1956.
35. Sills, M. A.; Wolfe, B. B.; Frazer, A. Determination of selective and nonselective compounds for the 5-HT1A and 5-HT1B receptor subtypes in rat frontal cortex. J. Pharmacol. Exp. Ther. 231:480–487; 1984.
36. Traber, J.; Davies, M. A.; Dompert, W. U.; Glaser, T.; Schuurman, T.; Seidel, P. R. Brain serotonin receptors as a target for the putative anxiolytic TVX Q 7821. Brain Res. Bull. 12:741–744; 1984.
37. Tricklebank, M. D.; Middlemiss, D. N.; Neill, J. Pharmacological analysis of the behavioural and thermoregulatory effects of the putative 5-HT1 receptor agonist, RU 24969, in the rat. Neuropharmacology 25:877–886; 1986.